

We claim:

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1. A method for treating an infectious disease caused by a bacteria, in an animal, comprising:

administering to an animal in need of such treatment, a lytic or non-lytic bacteriophage that is specific for said bacteria in a dosage effective to substantially eliminate the bacteria, wherein said bacteriophage has a genetically inheritable ability to delay inactivation by an animal's host defense system.

2. The method according to claim 1, wherein said bacteria is a drug resistant bacteria.

3. The method according to claim 1, wherein said animal is not a mammal.

4. The method according to claim 1, wherein said animal is a mammal.

5. The method according to claim 4, wherein said mammal is a human.

6. The method according to claim 1, wherein said bacteriophage has at least a 15% longer half-life than a corresponding wild-type phage.

7. The method according to claim 1, wherein the bacteriophage is obtained by anti-HDS selection (serial passage) of a mutagenized or non-mutagenized bacteriophage which is able to survive in an animal for a longer period than a corresponding wild-type bacteriophage.

8. The method according to claim 1, wherein the bacteria is selected from the group consisting of Mycobacteria, Staphylococci, Vibrio, Enterobacter, Enterococci, Escherichia, Haemophilus, Neisseria, Pseudomonas, Shigella, Serratia, Salmonella and Streptococci, and the bacteriophage can effectively lyse the bacteria.

9. The method according to claim 8, wherein the bacteria is selected from the group consisting of M. tuberculosis, M. avium-intracellulare and M. bovis.

10. The method according to claim 1, wherein the bacteriophage is administered by way of an aerosol to an animal's lungs.

11. The method according to claim 1, wherein the bacteriophage is administered at a dosage of about 10^6 to about 10^{13} pfu/kg/day.

12. The method according to claim 11, wherein the

bacteriophage is administered at a dosage of about 10^{12} pfu/kg/day.

13. An isolated and purified bacteriophage that has a genetically inheritable ability to delay inactivation by an animal's host defense system.

14. The bacteriophage according to claim 13, wherein said bacteriophage has at least a 15% longer half-life than a corresponding wild-type phage.

15. The bacteriophage according to claim 13, wherein the bacteriophage is obtained by anti-HDS selection of a bacteriophage that is able to survive in an animal's body longer than the corresponding wild-type bacteriophage.

16. The bacteriophage according to claim 13, wherein the bacteriophage is obtained by genetic engineering of an anti-HDS bacteriophage that is able to survive in an animal's body longer than the corresponding wild-type bacteriophage.

17. The bacteriophage according to claim 13, wherein said phage is specific for bacterial families selected from the group consisting of Escherichia, Klebsiella, Shigella, Salmonella, Serratia, Yersinia, Enterobacter, Enterococci, Haemophilus, Mycobacteria, Neisseria, Pseudomonas, Staphylococci, Streptococci and Vibrio.

18. A method of obtaining a bacteriophage that is able to delay inactivation by an animal's host defense system against foreign bodies, comprising:

- (a) intravenously injecting a bacteriophage into an animal;
- (b) obtaining serial blood samples over time and measuring the bacteriophage present in each sample;
- (c) growing a portion of a sample obtained when about 0.1% to 1% of the bacteriophage remain in said animal, to high titer in a host bacteria; and
- (d) repeating steps (a), (b) and (c) at least once, to yield an "anti-HDS" bacteriophage that has delayed inactivation by an animal's host defense system.

19. The method according to claim 18, wherein step (d) is repeated until a bacteriophage is obtained which has at least a 15% longer half-life than a corresponding wild-type phage.

20. A method of producing a bacteriophage able to delay inactivation by an animal's host defense system, comprising genetically engineering a bacteriophage to express molecules on its surface coat that delay inactivation of the bacteriophage by an animal's host defense system.

21. The method according to claim 1, wherein the bacteriophage

is obtained by genetic engineering.

22. The method according to claim 20, wherein the bacteria is selected from the group consisting of Mycobacteria, Staphylococci, Vibrio, Enterobacter, Enterococci, Escherichia, Haemophilus, Neisseria, Pseudomonas, Shigella, Serratia, Salmonella and Streptococci, and the bacteriophage can effectively lyse the bacteria.

23. The method according to claim 22, wherein the bacteria is selected from the group consisting of M. tuberculosis, M. avium-intracellulare and M. bovis.

24. The method according to claim 20, wherein the bacteriophage is administered by way of an aerosol to an animal's lungs.

25. The method according to claim 20, wherein the bacteriophage is administered at a dosage of about 10^6 to about 10^{13} pfu/kg/day.

26. The method according to claim 25, wherein the bacteriophage is administered at a dosage of about 10^{12} pfu/kg/day.

27. A method for treating an infectious disease caused by a bacteria, comprising administering to an animal in need of such

treatment an antibiotic and/or a chemotherapeutic agent in combination with a bacteriophage specific for said bacteria, in a dosage effective to substantially eliminate the bacteria, wherein said bacteriophage has a genetically inheritable ability to delay inactivation by the animal's host defense system.

28. A pharmaceutical composition comprising an isolated and purified bacteriophage which has a genetically inheritable ability to delay inactivation by an animal's host defense system, in combination with a pharmaceutically acceptable carrier.

29. The pharmaceutical composition according to claim 28, wherein said composition is an aerosol formulation for administration to an animal's lungs.

30. The pharmaceutical composition according to claim 28, wherein said bacteriophage is in lyophilized form.

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